

Infections and infectious diseases

Principles and basic mechanisms

Principles and basic mechanisms

- **Pathogenicity** ;- is the capability of an organism to cause disease.
- **Virulence** :- is the extent to which a pathogen is able to cause disease.
- **Pathogens produce proteins and other factors, termed virulence factors, which contribute to disease.**
- **Primary pathogens** cause disease in a proportion of individuals to whom they are exposed, regardless of the host's immunological status.
- **Opportunistic pathogens** cause disease only in individuals whose host defenses are compromised, e.g. by an intravascular catheter, or when the immune system is compromised, by genetic susceptibility or immunosuppressive therapy.

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❖ Characteristics of successful pathogens :-

- They compete with host cells and colonizing flora by various methods, including :
 - ✓ Sequestration of nutrients.
 - ✓ Production of bacteriocins.
- Motility enables pathogens to reach their site of infection, often sterile sites that colonizing bacteria do not reach, such as the distal airway.
- Many microorganisms, including viruses, use 'adhesins' to attach to host cells initially.
- Some pathogens can invade through tissues.

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❖ Characteristics of successful pathogens :-

- Many bacterial and fungal infections form 'biofilms'.
- After initial adhesion to a host surface, bacteria multiply in biofilms to form complex surrounded by a matrix of host and bacterial products that afford protection to the colony and limit the effectiveness of antimicrobials.
- Biofilms forming on man-made medical devices such as vascular catheters or grafts can be particularly difficult to treat.
- Pathogens may produce toxins, microbial molecules that cause adverse effects on host cells, either at the site of infection, or remotely following carriage through the blood stream.

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❖ Characteristics of successful pathogens :-

- Endotoxin is the lipid component of Gram-negative bacterial outer membrane lipopolysaccharide.
- It is released when bacterial cells are damaged and has generalized inflammatory effects.
- Exotoxins are proteins released by living bacteria, which often have specific effects on target organs.
- Intracellular pathogens, including viruses, bacteria (e.g. *Salmonella* spp., *Mycobacterium tuberculosis*), parasites (e.g. *Leishmania* spp.) and fungi (e.g. *Histoplasma capsulatum*), are able to survive in intracellular environments, including after phagocytosis by macrophages.

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❖ Characteristics of successful pathogens :-

- Pathogenic bacteria express different genes, depending on environmental stress (pH, iron starvation, O₂ starvation etc.) and anatomical location.
- Genetic diversity enhances the pathogenic capacity of bacteria.
- Some virulence factor genes are found on plasmids or in phages and are exchanged between different strains or species.
- The ability to acquire genes from the gene pool of all strains of the species (the 'bacterial supragenome') increases diversity and the potential for pathogenicity.

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❖ Characteristics of successful pathogens :-

- **Viruses exploit their rapid reproduction and potential to exchange nucleic acid with host cells to enhance diversity.**
- **Once a strain acquires a particularly effective combination of virulence genes, it may become an epidemic strain, accounting for a large subset of infections in a particular region.**
- **This phenomenon accounts for influenza pandemics.**

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❖ Pathogenesis of infectious disease :-

❖ The host response :-

- Innate and adaptive immune and inflammatory responses, which humans use to control the normal flora and respond to pathogens.
- The harmful manifestations of infection are determined by a combination of the virulence of the organism and the host response to infection.
- Despite the obvious benefits of an intact host response, an excessive response is undesirable.
- Cytokines and antimicrobial factors contribute to tissue injury at the site of infection, and an excessive inflammatory response may lead to hypotension and organ dysfunction.

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❖ Pathogenesis of infectious disease :-

❖ The host response :-

- The contribution of the immune response to disease manifestations is exemplified by the immune reconstitution inflammatory syndrome (IRIS).
- This is seen, for example in :-
 - ✓ Human immunodeficiency virus (HIV) infection.
 - ✓ Post-transplantation neutropenia.
 - ✓ Tuberculosis (which causes suppression of T-cell function).
- Is a paradoxical worsening of the clinical condition as the immune dysfunction is corrected, caused by an exuberant but dysregulated inflammatory response.

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❖ The febrile response :-

- Thermoregulation is altered in infectious disease, which may cause both hyperthermia (fever) and hypothermia.
- Fever is mediated mainly by 'pyrogenic cytokines' (e.g. interleukins IL-1 and IL-6, and tumour necrosis factor alpha (TNF- α)).
- 'Pyrogenic cytokines' are released in response to various immunological stimuli including activation of pattern recognition receptors by microbial pyrogens and factors released by injured cells.
- Their ultimate effect is to induce the synthesis of prostaglandin E₂, which binds to specific receptors in the preoptic nucleus of the hypothalamus (thermoregulatory center), causing the core temperature to rise.

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❖ The febrile response :-

- Rigors are a clinical symptom characterized by feeling very cold ('chills') and uncontrollable shivering, usually followed by fever and sweating.
- Rigors occur when the thermoregulatory center attempts to correct a core temperature to a higher level by stimulating skeletal muscle activity and shaking.
- There are data to support the hypothesis that raised body temperature interferes with the replication and/or virulence of pathogens.
- The mechanisms and possible protective role of infection-driven hypothermia, however, are poorly understood, and require further study.

Good Luck